This listing of claims will replace all prior versions, and listings, of claims in the application:

## **LISTING OF CLAIMS:**

1. (Currently Amended) A compound of Formula I:

$$A - D - B \tag{I}$$

or a pharmaceutically acceptable salt thereof, wherein

D is 
$$-NH-C(O)-NH-$$
,

A is a substituted moiety of up to 40 carbon atoms of the formula: L (M L<sup>1</sup>)<sub>q</sub>, where L is a 5 or 6 membered cyclic structure bound directly to D, L<sup>1</sup> comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L<sup>1</sup> contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6 member cyclic structure bound directly to D containing 0 4 members of the group consisting of nitrogen, oxygen and sulfur, wherein L<sup>1</sup> is substituted by at least one substituent selected from the group consisting of SO<sub>2</sub>R<sub>x</sub>, C(O)R<sub>x</sub> and C(NR<sub>y</sub>) R<sub>x̄</sub>.

R<sub>y</sub> is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R<sub>z</sub> is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and

carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

 $OSi(R_f)_3$ -where  $R_f$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

e) one of  $R_a$  or  $R_b$  is C(O), a  $C_1$ - $C_5$ -divalent alkylene group or a substituted  $C_1$ - $C_5$ -divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1$ - $C_5$ -divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L<sup>1</sup> is additionally substituted, the substituents are selected from the group consisting of halogen, up to per halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, C(O) R<sup>7</sup>, NO<sub>2</sub>, OR<sup>7</sup>, SR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, Q Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, OR<sup>7</sup>, SR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, NO<sub>2</sub>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup> and halogen up to per halo; with each R<sup>7</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

Ar is a 5 or 6 member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per halo, and optionally substituted by  $Z_{n1}$ , wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of CN,  $CO_2R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ , and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of CN,  $CO_2R^7$ ,  $COR^7$ ,  $COR^$ 

## A is a substituted moiety of the formula:

# $-L-M-L^1$ ,

wherein L is a phenyl, pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, triazolyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl or triazinyl, and L is optionally substituted by halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of  $\underline{C_1}$ - $\underline{C_5}$  linear or branched alkyl,  $\underline{C_1}$ - $\underline{C_5}$  linear or branched haloalkyl up to perhalo,  $\underline{C_1}$ - $\underline{C_3}$  alkoxy,  $\underline{C_1}$ - $\underline{C_3}$  haloalkoxy up to per haloalkoxy, hydroxy, amino,  $\underline{C_1}$ - $\underline{C_3}$  alkylamino,  $\underline{C_1}$ - $\underline{C_6}$  dialkylamino, halogen, -CN, and -NO<sub>2</sub>;

earbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, OR<sup>7</sup>, SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, NO<sub>2</sub>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>2</sup>C(O)OR<sup>7</sup> and halogen up to per halo;

with each R<sup>2</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

# L<sup>1</sup> comprises a substituted cyclic moiety selected from the group consisting of:

(i) phenyl, naphthyl, pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, triazolyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, benzoxazolyl, quinolinyl, isoquinolinyl, benzofuryl, benzothiazolyl, indolyl, benzimidazolyl, benzopyrazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzoxadiazolyl and quinazolinyl,

optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)OR<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano and nitro;

wherein L<sup>1</sup> is substituted by  $-C(O)R_x$ ,

wherein R<sub>x</sub> is R<sub>z</sub> or NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are

## A) independently

- a) hydrogen,
- b)  $C_1$ - $C_{10}$  alkyl,
- c) C<sub>3-10</sub> cycloalkyl, having 0-3 heteroatoms selected from N, S and O
- d)  $C_6$  aryl,
- e) C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from O, N and S,
- f) substituted  $C_{1-10}$  alkyl,
- g) substituted C<sub>3-10</sub> cycloalkyl, having 0-3 heteroatoms selected from N, S and O,
- h) substituted  $C_6$  aryl,
- i) substituted C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O,
- j) -phenylpiperazine(pyridyl) or
- k)  $-C_2H_4NH(phenyl)$ ;

## where R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by

- a) halogen up to per halo,
- b) hydroxy,
- c)  $-N(CH_3)_2$ ,
- d)  $C_1$ - $C_{10}$  alkyl,
- e)  $C_1$ - $C_{10}$  alkoxy,
- f) C<sub>3-12</sub> cycloalkyl, having 1-3 heteroatoms selected from O, N and S,

- g) halosubstituted C<sub>1-6</sub> alkyl, or
- h)  $-OSi(Pr-i)_3$ ;
- B)  $R_a$  and  $R_b$  together form piperazine or a substituted piperizine with substituents selected from the group consisting of
  - a) halogen,
  - b) hydroxy,
  - c)  $C_{1-10}$  alkyl,
  - d) C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N,
  - e) C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O,
  - f)  $C_{1-10}$  alkoxy,
  - g)  $C_6$  aryl,
  - h) halo substituted  $C_{1-6}$  alkyl up to per halo alkyl,
  - i) halo substituted C<sub>6</sub> aryl up to per halo aryl,
  - j) N-(4-acetylphenyl);
  - k) halo substituted C<sub>3</sub>-C<sub>12</sub> cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, and
  - l) halo substituted C<sub>3</sub>-C<sub>12</sub> hetaryl up to per halo heteraryl,

or

C) one of  $R_a$  or  $R_b$  is -C(O)- bound to the moiety  $L^1$  to form an isoindoline-1, 3-dione structure or a  $C_1$  divalent alkylene group or a substituted  $C_1$  divalent alkylene group bound to the moiety  $L^1$  to form a 1-oxo-isoindoline structure,

wherein the substituents of the substituted C<sub>1</sub> divalent alkylene group are selected from the group consisting of

- a) halogen,
- b) hydroxy,
- c)  $C_{1-10}$  alkyl,
- d) C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N,
- e) C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O,
- $\underline{f}$   $C_{1-10}$  alkoxy,
- g)  $C_6$  aryl,
- h) halo substituted C<sub>1-6</sub> alkyl up to per halo alkyl,

- i) halo substituted C<sub>6</sub>aryl up to per halo aryl,
- j) halo substituted C<sub>3</sub>-C<sub>12</sub> cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, and
- k) halo substituted C<sub>3</sub>-C<sub>12</sub> hetaryl up to per halo heteroaryl;

# M is selected from the group consisting of

-(CH<sub>2</sub>)<sub>m</sub>-O-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-S-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-N(R<sup>7</sup>)-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-C(O)-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-CH(OH)-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-(CH<sub>2</sub>)<sub>1</sub>-,

-(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-(CH<sub>2</sub>)<sub>1</sub>-,

 $-(CH_2)_m - N(R^7)C(O) - (CH_2)_1 - and$ 

 $-(CH_2)_m - C(O)N(R^7) - (CH_2)_1 -$ 

where m and l are each independently integers of from 1-3, and X is halogen; and

B is selected from the group consisting of:

- (i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup> halogen, cyano, and nitro;
- (ii) naphthyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano, and nitro;
- (iii) pyridinyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano, and nitro; and

August 16, 2004

Submission Filed With RCE

(iv) quinolinyl or isoquinolinyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)OR<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano, and nitro;

each R7, R7, R2 is independently

- (a) hydrogen,
- (b)  $C_1$ - $C_6$  linear, branched, or cyclic alkyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy and hydroxy;
- (c)  $C_1$ - $C_6$  linear or branched, alkoxy, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen;
- (d) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen,
- (e) 5-6 membered monocyclic heteroaryl having 1-4 heteroatoms selected from the group consisting of O, N and S or 8-10 membered bicyclic heteroaryl having 1-6 heteroatoms selected from the group consisting of O, N and S, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen,
- (f)  $C_1$ - $C_3$  alkyl-phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen; and
- (g) up to per-halo substituted  $C_1$ - $C_5$  linear, branched or cyclic alkyl, and where not per-halo substituted, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy and hydroxy.

## 2. (Canceled)

3. (Currently Amended) A compound as in claim 1 wherein M is one or more bridging groups selected from the group consisting of  $\frac{O}{O}$ ,  $\frac{S}{O}$ ,  $\frac{N(R^7)}{O}$ ,  $\frac{CH_2}{O}$ ,

-C(O), -CH(OH),  $-(CH_2)_mO$ ,  $-(CH_2)_mS$ ,  $-(CH_2)_mN(R^7)$ ,  $-O(CH_2)_m$ ,  $-CHX^0$ ,  $-CX^0_2$ , -S $(CH_2)$  and  $N(R^7)(CH_2)_m$ ,  $(CH_2)_m$ , where m=1-3,  $X^a$  is halogen and  $-O_{-}$ ,  $-S_{-}$ ,  $-N(R^{7})_{-}$ ,  $-C(O)_{-}$ ,  $-CH(OH)_{-}$ ,  $-(CH_{2})O_{-}$ ,  $-(CH_{2})S_{-}$ ,  $-(CH_{2})N(R^{7})_{-}$ ,  $-O(CH_{2})_{-}$ ,  $-CHF_{-}$ ,  $-CF_2$ ,  $-S-(CH_2)$ - and  $-N(R^7)(CH_2)$ -,  $-C(O)CH_2$ -,  $-CH_2OC(O)$ -,  $-C(O)OCH_2$ -,  $-C(O)N(R^7)CH_{2-}$ ,  $-N(R^7)C(O)CH_{2-}$ ,  $-N(R^7)C(O)OCH_{2-}$ , where  $R^7$  is as defined in claim 1.

- (Original) A compound as in claim 1 wherein the cyclic structures of B and L 4. bound directly to D are not substituted in the ortho position by-OH.
  - 5. (Canceled)
  - (Original) A compound of claim 1 wherein B of Formula I is 6.
- phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup> halogen, cyano, and nitro; or
- (ii) pyridinyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano, and nitro a substituted or unsubstituted six member aryl moiety or six member hetaryl moiety, said hetaryl moiety having 1 to 4 members selected from the group of hetaryl atoms consisting of nitrogen, oxygen and sulfur with the balance of the hetaryl moiety being carbon.
- 7. (Currently Amended) A compound of claim 1 wherein B of Formula I is phenyl, substituted with 1-3 substituents independently selected from the group consisting of nitro; or

 $C_1$ - $C_{10}$  alkyl,

 $C_1$ - $C_{10}$  alkoxy,

C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

 $C_6$  aryl,

C<sub>3</sub>-C<sub>12</sub> hetaryl having 1-3 heteroatoms selected from O, N and S,

substituted  $C_1$ - $C_{10}$  alkyl, substituted by one or more substituents independently selected from the group consisting of halogen, up to per halo, and -OR<sup>7</sup>, where R<sup>7</sup> is H or  $C_{1-10}$  alkyl;

substituted  $C_1$ - $C_{10}$  alkoxy, substituted by one or more substituents independently selected from the group consisting of halogen, up to per halo, and  $-OR^7$ , where  $R^7$  is H or  $C_{1-10}$  alkyl;

substituted  $C_3$ - $C_{10}$  cycloalkyl, substituted by one or more substituents independently selected from the group consisting of halogen, up to per halo, and -OR<sup>7</sup>, where R<sup>7</sup> is H or  $C_{1-10}$  alkyl;

substituted  $C_6$  aryl, substituted by one or more substituents independently selected from the group consisting of halogen, up to per halo, and  $-OR^7$ , where  $R^7$  is H or  $C_{1-10}$  alkyl;

substituted  $C_3$ - $C_{12}$  hetaryl having 1-3 heteroatoms selected from O, N and S, substituted by one or more substituents independently selected from the group consisting of halogen, up to per halo, and -OR<sup>7</sup> where R<sup>7</sup> is H or  $C_{1-10}$  alkyl;

-CN; -OR<sup>7</sup>; CO<sub>2</sub>R<sup>7</sup>, -CO(NR<sup>7</sup>R<sup>7</sup>), -C(O)R<sup>7</sup>, NO<sub>2</sub>, NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, wherein R<sup>7</sup> is hydrogen or C<sub>1-10</sub> alkyl an unsubstituted phenyl group, an unsubstituted pyridyl group, an unsubstituted pyrimidinyl, a phenyl group substituted by a substituent selected from the group consisting of halogen and Wn wherein W and n are as defined in claim 1, a pyrimidinyl group substituted by a substituent selected from the group constituting of halogen and Wn, whereas W and n are as defined in Claim 1, or a substituted pyridyl group substituted by a substituent selected from the group consisting of halogen and Wn wherein W and n are as defined in claim 1.

8. (Currently Amended) A compound of claim 6 wherein B of Formula I is a substituted phenyl group, a substituted pyrimidinyl group, or substituted pyridyl group phenyl, substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen,  $C_1$ - $C_6$   $C_{10}$  alkyl,  $C_1$ - $C_6$   $C_{10}$  alkoxy, -OH, up to per halo substituted  $C_1$ - $C_6$   $C_{10}$  alkoxy or phenyl substituted by halogen up to per halo.

# 9. (Currently Amended) A compound of claim 1, wherein L is

phenyl, optionally substituted by halogen up to perhalo and Wn, where n and W are as defined in claim 1, the six member cyclic structure bound directly to D, is a substituted or unsubstituted 6 member aryl moiety or a substituted or unsubstituted 6 member hetaryl moiety, wherein said hetaryl moiety has 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur with the balance of said hetaryl moiety being carbon, wherein the one or more substituents are selected from the group consisting of halogen and Wn wherein W and n are as defined in claim 1.

- 10. (Currently Amended) A compound of claim 8, wherein L is
- (i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> halosubstituted alkyl and C<sub>1</sub>-C<sub>6</sub> alkoxy, the 6 member cyclic structure bound directly to D, is a substituted phenyl, unsubstituted phenyl, substituted pyrimidinyl, unsubstituted pyrimidinyl, substituted pyridyl or unsubstituted pyridyl group.
- 11. (Currently Amended) A compound of claim 1, wherein said substituted eyelic moiety L<sup>1</sup> is
- (i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, halogen, cyano and nitro; or
- (ii) pyridinyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano and nitro comprises a 5 to 6 membered aryl moiety or hetaryl moiety, wherein said heteraryl moiety comprises 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur.
- 12. (Currently Amended) A compound of claim 1, wherein said substituted eyelic moiety L<sup>1</sup> is phenyl or[[,]] pyridinyl or pyrimidinyl.

- 13. (Currently Amended) A compound of claim 7 3, wherein said substituted eyelic moiety  $L^1$  is phenyl or[[,]] pyridinyl or pyrimidinyl.
- 14. (Currently Amended) A compound of claim 6, wherein said substituted eyelic moiety  $L^1$  is phenyl or[[,]] pyridinyl or pyrimidinyl.
- 15. (Currently Amended) A compound of claim 8, wherein said substituted eyelic moiety L<sup>1</sup> is phenyl or[[,]] pyridinyl or pyrimidinyl.
- 16. (Currently Amended) A compound of claim 9, wherein said substituted eyelic moiety L<sup>1</sup> is phenyl or[[,]] pyridinyl or pyrimidinyl.
- 17. (Currently Amended) A compound of claim 10, wherein said substituted eyelic moiety L<sup>1</sup> is phenyl or[[,]] pyridinyl or pyrimidinyl.
- bridging groups selected from the group consisting of <u>O- or -S-</u> where R<sup>7</sup> is as defined in elaim 1 O, S N(R<sup>7</sup>), (CH<sub>2</sub>)<sub>m</sub> , C(O), CH(OH), (CH<sub>2</sub>)<sub>m</sub>O, (CH<sub>2</sub>)<sub>m</sub>S, (CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>), O(CH<sub>2</sub>)<sub>m</sub> CHX<sup>a</sup>, CX<sup>a</sup><sub>2</sub>, S (CH<sub>2</sub>)<sub>m</sub> and N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.
- bridging groups selected from the group consisting of <u>O- or -S- O, S- and, N(R<sup>7</sup>), (CH<sub>2</sub>)<sub>m</sub>, C(O), CH(OH), (CH<sub>2</sub>)<sub>m</sub>O, (CH<sub>2</sub>)<sub>m</sub>S, (CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>), O(CH<sub>2</sub>)<sub>m</sub> CHX<sup>a</sup>, CCX<sup>a</sup><sub>2</sub>, S (CH<sub>2</sub>)<sub>m</sub> and N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.</u>

- 20. (Currently Amended) A compound of claim 16, wherein M is one or more bridging groups selected from the group consisting of  $\underline{\text{-O- or -S-}}$   $\underline{\text{-O , S- and, N(R}^7)}$ ,  $\underline{\text{-(CH}_2)_m}$ , where  $\underline{\text{m- 1- 3, X}^a}$  is halogen and  $\underline{\text{R}^7}$  is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.
- 21. (Currently Amended) A compound of claim 17, wherein M is one or more bridging groups selected from the group consisting of <u>O- or -S- O-, S- and, N(R<sup>7</sup>)</u>, (CH<sub>2</sub>)<sub>m</sub>, C(O), CH(OH), (CH<sub>2</sub>)<sub>m</sub>O-, (CH<sub>2</sub>)<sub>m</sub>S-, (CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>), O(CH<sub>2</sub>)<sub>m</sub> CHX<sup>a</sup>, CX<sup>a</sup><sub>2</sub>, S (CH<sub>2</sub>)<sub>m</sub> and N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.
- **22.** (Currently Amended) A compound of claim  $\underline{12}$  4 wherein  $L^1$  is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.
- 23. (Currently Amended) A compound of claim  $\underline{14}$   $\underline{13}$  wherein  $L^1$  is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.
- **24.** (Currently Amended) A compound of claim  $\underline{15}$  18 wherein  $L^1$  is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.
- 25. (Currently Amended) A compound of claim 16 19 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group

consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.

- **26.** (Currently Amended) A compound of claim 17 20 wherein  $L^1$  is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.
- **27.** (Original) A compound of claim 21 wherein  $L^1$  is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.

## 28.-32. (Canceled)

- 33. (Currently Amended) A compound of claim 13 wherein  $L^1$  is substituted by  $-C(O)R_x$ , wherein  $R_x$  is  $NR_aR_b$ , and  $R_a$  and  $R_b$  are independently <u>hydrogen</u>,  $C_1$ - $C_6$  alkyl or  $C_1$ - $C_6$  alkoxy
  - a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

 $-OSi(R_f)_3$ -where  $R_f$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5.7 member heterocyclic structure of 1.3 heteroatoms selected from N, S and O, or a substituted 5.7 member heterocyclic structure of 1.3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based

substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

- e) one of  $R_a$  or  $R_b$  is -C(O), a  $C_1$ - $C_5$ -divalent alkylene group or a substituted  $C_1$ - $C_5$ -divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1$ - $C_5$ -divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.
- 34. (Currently Amended) A compound of claim  $\underline{14}$  18 wherein  $L^1$  is substituted by  $-C(O)R_x$ , wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently <u>hydrogen</u>,  $C_1$  <u>-C6 alkyl or C1 -C6 alkoxy hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.</u>
- 35. (Currently Amended) A compound of claim  $\underline{15}$  19 wherein  $L^1$  is substituted by  $-C(O)R_x$ , wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently <u>hydrogen</u>,  $C_1$ — $C_6$  alkyl or  $\underline{C_1}$ — $C_6$  alkoxy hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.
- 36. (Currently Amended) A compound of claim  $\underline{16}$  20 wherein  $L^1$  is substituted by  $-C(O)R_x$ , wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently <u>hydrogen</u>,  $C_1$ — $C_6$  alkyl or  $\underline{C_1}$ — $C_6$  alkoxy hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

37. (Currently Amended) A compound of claim  $\underline{17}$  21 wherein  $L^1$  is substituted by  $-C(O)R_x$ , wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently <u>hydrogen</u>,  $C_1$  <u>-C6 alkyl or C1 -C6 alkoxy hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.</u>

## 38. (Currently Amended) A compound of Formula I:

$$A - D - B \tag{I}$$

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: L (M L<sup>1</sup>)<sub>q</sub>, where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D, L<sup>1</sup> comprises a substituted cyclic moiety having at least 5 members, M is abridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L<sup>1</sup> contains 0 4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6 member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein  $L^1$  is substituted by at least one substituent selected from the group consisting of  $SO_2R_*$ ,  $-C(O)R_*$  and  $-C(NR_y)$   $R_z$ ,  $R_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

R<sub>z</sub> is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R<sub>\*</sub> is R<sub>2</sub> or NR<sub>6</sub>R<sub>5</sub> where R<sub>6</sub> and R<sub>5</sub> are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and

carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

OSi(R<sub>f</sub>)<sub>3</sub>-where R<sub>f</sub> is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

e) one of  $R_a$  or  $R_b$  is -C(O), a  $C_1$ - $C_5$ -divalent alkylene group or a substituted  $C_1$ - $C_5$ -divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1$ - $C_5$ -divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L<sup>1</sup> is additionally substituted, the substituents are selected from the group consisting of halogen, up to per halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>2</sup>; C(O)NR<sup>2</sup>R<sup>2</sup>, C(O) R<sup>2</sup>, NO<sub>2</sub>, OR<sup>2</sup>, SR<sup>2</sup>, NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>C(O)OR<sup>2</sup>, NR<sup>2</sup>C(O)R<sup>2</sup>, Q Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>2</sup>, C(O)R<sup>2</sup>, C(O)NR<sup>2</sup>R<sup>2</sup>, OR<sup>2</sup>, SR<sup>2</sup>; NR<sup>2</sup>R<sup>2</sup>, NO<sub>2</sub>, NR<sup>2</sup>C(O)R<sup>2</sup>, NR<sup>2</sup>C(O)OR<sup>2</sup> and halogen up to per halo; with each R<sup>2</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

Ar is a 5- or 6 member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per halo, and optionally substituted by  $Z_{n1}$ , wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of CN,  $CO_2R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ ,  $C(O)R^7$ , and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents are selected from the group consisting of CN,  $CO_2R^7$ ,  $COR^7$ ,  $CO_2R^7$ ,  $COR^7$ ,  $CO_2R^7$ , CO

wherein M is one or more bridging groups selected from the group consisting of O, S,  $-N(R^7)$ ,  $-(CH_2)_m$ , -C(O), -CH(OH),  $-(CH_2)_mO$ ,  $-(CH_2)_mS$ ,  $-(CH_2)_mN(R^7)$ ,  $-O(CH_2)_m$ - $-(CH_2)_m$ , where  $-(CH_2)_m$  is halogen

A is of the formula: -L-M-L<sup>1</sup>, wherein

L is

(i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_5$  linear or branched haloalkyl up to perhalo,  $C_1$ - $C_3$  alkoxy,  $C_1$ - $C_3$  haloalkoxy up to per haloalkoxy, hydroxy, amino,  $C_1$ - $C_3$  alkylamino,  $C_1$ - $C_6$  dialkylamino, halogen, cyano, and nitro;

L<sup>1</sup> comprises a substituted cyclic moiety selected from the group consisting of:

- (i) phenyl, optionally substituted by 1-3 substituents which are independently methyl or halogen; or
- (ii) pyridinyl, substituted with 1-3 substituents which are independently methyl or halogen;

wherein  $L^1$  is substituted by  $-C(O)R_x$ ,

wherein R<sub>x</sub> is R<sub>z</sub> or NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are independently

hydrogen,

 $C_1$ - $C_{10}$  alkyl,

 $C_6$  aryl,

C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from O, N and S,

substituted C<sub>1-10</sub> alkyl,

substituted C<sub>3-10</sub> cycloalkyl, having 0-3 heteroatoms selected from N, S and O,

August 16, 2004

Submission Filed With RCE

## substituted C<sub>6</sub> aryl, or

substituted C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O,

where R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by halogen up to per halo. and

M is selected from the group consisting of -O-, -S-, -NHC(O)- and -C(O)NH-,

q is 1: and

## B is selected from the group consisting of:

- (i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup> halogen, cyano, and nitro;
- (ii) pyridyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R<sup>7</sup>, OR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)OR<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, halogen, cyano, and nitro; and

each R<sup>7</sup>, R<sup>7</sup>, R<sub>z</sub> and R<sub>f</sub> is independently

## (a) hydrogen,

- (b)  $C_1$ - $C_6$  linear, branched, or cyclic alkyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy and hydroxy;
- (c)  $C_1$ - $C_6$  linear or branched, alkoxy, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen;
- (d) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen,
- (e) 5-6 membered monocyclic heteroaryl having 1-4 heteroatoms selected from the group consisting of O, N and S or 8-10 membered bicyclic heteroaryl having 1-6 heteroatoms selected from the group consisting of O, N and S, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen,

- (f)  $C_1$ - $C_3$  alkyl-phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy, hydroxy and halogen; and
- (g) up to per-halo substituted  $C_1$ - $C_5$  linear, branched or cyclic alkyl, and where not per-halo substituted, optionally substituted with 1-3 substituents independently selected from the group consisting of  $C_1$ - $C_5$  linear or branched alkyl, up to perhalo substituted  $C_1$ - $C_5$  linear or branched alkyl,  $C_1$ - $C_3$  alkoxy and hydroxy.

## **39.** (Currently Amended) A compound of Formula I:

$$A - D - B \tag{I}$$

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: L (M L<sup>1</sup>)<sub>q</sub>, where L is a substituted or unsubstituted phenyl or moiety bound directly to D,L<sup>1</sup> comprises a substituted phenyl, or pyrimidinyl moiety, M is bridging group having at least one atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted phenyl or group bound directly to D,

wherein L<sup>1</sup> is substituted by at least one substituent selected from the group consisting of SO<sub>2</sub>R<sub>x</sub>, C(O)R<sub>x</sub> and C(NR<sub>y</sub>) R<sub>z</sub>,

R<sub>y</sub> is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo, and;

 $R_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

Rx is Rz or NRaRb where Ra and Rb are

# a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and

carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

 $-OSi(R_f)_3$  where  $R_f$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

e) one of R<sub>a</sub> or R<sub>b</sub> is -C(O), a C<sub>1</sub> C<sub>5</sub> divalent alkylene group or a substituted C<sub>1</sub>-C<sub>5</sub> divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C<sub>1</sub>-C<sub>5</sub> divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L<sup>1</sup> is additionally substituted, the substituents are selected from the group consisting of halogen, up to per halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O) R<sup>7</sup>, NO<sub>2</sub>, OR<sup>7</sup>, SR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup>, NR<sup>7</sup>C(O)R<sup>7</sup>, Q Ar, and earbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of CN, CO<sub>2</sub>R<sup>7</sup>, C(O)R<sup>7</sup>, C(O)NR<sup>7</sup>R<sup>7</sup>, OR<sup>7</sup>, SR<sup>7</sup>, NR<sup>7</sup>R<sup>7</sup>, NO<sub>2</sub>, NR<sup>7</sup>C(O)R<sup>7</sup>, NR<sup>7</sup>C(O)OR<sup>7</sup> and halogen up to per halo; with each R<sup>7</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is O, S,  $N(R^7)$ ,  $(CH_2)_m$ , C(O), CH(OH),  $(CH_2)_mO$ ,  $(CH_2)_mS$ ,  $(CH_2)_mN(R^7)$ ,  $O(CH_2)_m$   $CHX^6$ ,  $CX^6_2$ , S,  $(CH_2)_m$  and  $N(R^7)(CH_2)_m$ , where m=1-3, and  $X^6$  is halogen;

A is of the formula:

$$-L-M-L^1$$
,

where L is

M is

and l are each independently integers of from,

$$O_{+} - S_{+} - N(R^{7})_{+} + (CH_{2})_{m} - C(O)_{+} - CH(OH)_{+} + (CH_{2})_{m}O_{+} - (CH_{2})_{m}S_{+} - (CH_{2})_{m}N(R^{7})_{+} - (CH_{2})_{m} - CHX^{6}_{-} - CX^{6}_{2}_{-} - S_{-}(CH_{2})_{m} - and_{-} - N(R^{7})(CH_{2})_{m}_{-} + where m = 1-3,$$

and

B-is

L is phenyl,

M is -O-,

L<sup>1</sup> is pyridinyl substituted by  $-C(O)R_x$ wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently hydrogen,

 $C_1$ - $C_{10}$  alkyl,

 $C_1$ - $C_{10}$  alkoxy,

C<sub>3-10</sub> cycloalkyl,

 $C_6$  aryl,

C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from O, N and S,

substituted C<sub>1-10</sub> alkyl,

substituted  $C_{1-10}$  alkoxy,

substituted C<sub>3-10</sub> cycloalkyl, having 0-3 heteroatoms selected from N, S and O,

substituted C<sub>6</sub> aryl, or

substituted C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O,

where Ra and Rb are a substituted group, they are substituted by

halogen up to per halo, and

B is a phenyl group substituted by substituents selected from the group consisting of hydrogen up to per halo, and W where n is 0-3, and each W is independently selected from the group consisting of

 $C_1$ - $C_{10}$  alkyl,

 $C_1$ - $C_{10}$  alkoxy,

C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

 $C_6$  aryl,

C<sub>3</sub>-C<sub>12</sub> heteroaryl having 1-3 heteroatoms selected from O, N and S,

substituted  $C_1$ - $C_{10}$  alkyl, substituted by one or more substituents independently selected from the group consisting of -OR<sup>7</sup> and halogen up to per halo, wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_{10}$  alkyl;

substituted  $C_1$ - $C_{10}$  alkoxy, substituted by one or more substituents independently selected from the group consisting of -OR<sup>7</sup> and halogen up to per halo, wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_{10}$  alkyl;

substituted  $C_3$ - $C_{10}$  cycloalkyl, substituted by one or more substituents independently selected from the group consisting of -OR<sup>7</sup> and halogen up to per halo, wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_{10}$  alkyl;

substituted  $C_6$  aryl, substituted by one or more substituents independently selected from the group consisting of  $-OR^7$  and halogen up to per halo, wherein  $R^7$  is hydrogen or  $C_{10}$  alkyl;

substituted  $C_3$ - $C_{12}$  heteroaryl having 1-3 heteroatoms selected from O, N and S, substituted by one or more substituents independently selected from the group consisting of  $-OR^7$  and halogen up to per halo, wherein  $R^7$  is hydrogen or  $C_1$ - $C_{10}$  alkyl;

-CN,

 $-CO_2R^7$ 

 $-C(O)NR^7R^7$ ,

 $-C(O)R^7$ ,

 $-NO_2$ 

 $-OR^7$ ,

 $-NR^7R^7$ 

-NR<sup>7</sup>C(O)OR<sup>7</sup> and

-NR<sup>7</sup>C(O)R<sup>7</sup>, wherein R<sup>7</sup> is hydrogen, or C<sub>1</sub>-C<sub>10</sub> alkyl.

40. (Original) A compound as in claim 38 wherein the cyclic structures of B and L bound directly to D are not substituted in the ortho position by-OH.

## 41. (Canceled)

42. (Original) A compound as in claim 39 wherein the cyclic structures of B and L bound directly to D are not substituted in the ortho position by-OH.

## 43. (Canceled)

- 44. (Currently Amended) A compound as in claim 38 wherein substituents for B and L and additional substituents for L<sup>1</sup>, are selected from the group consisting of  $C_1$ - $\underline{C_6}$ - $C_{10}$  alkyl up to per halo substituted  $C_1$ - $\underline{C_6}$ - $C_{10}$  alkyl, CN, OH, halogen,  $C_1$ - $\underline{C_6}$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $\underline{C_6}$ - $C_{10}$  alkoxy.
- 45. (Currently Amended) A compound as in claim 39 wherein substituents for B and L and additional substituents for L<sup>1</sup>, are selected from the group consisting of  $C_1$ - $C_6$   $C_{10}$

alkyl up to per halo substituted  $C_1$ - $\underline{C_6}$ - $C_{10}$  alkyl, CN, OH, halogen,  $C_1$ - $\underline{C_6}$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $\underline{C_6}$   $C_{10}$  alkoxy.

## 46. (Canceled)

## 47. (Canceled)

- 48. (Currently Amended) A compound of claim 46  $\underline{38}$  wherein  $R_*$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently  $R_z$ .
- 49. (Currently Amended) A compound of claim 47  $\underline{39}$  wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently  $R_z$ .
- 50. (Currently Amended) A compound of claim 1 which is a pharmaceutically acceptable salt of a compound of formula I of claim 1 which is
- a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or
- b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

#### selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p toluene sulphonic acid (tosylate salt), 1 napthalene sulfonic acid, 2 napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid,

August 16, 2004

Submission Filed With RCE

fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

- b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.
- 51. (Currently Amended) A compound of claim 2 which is a pharmaceutically acceptable salt of a compound of claim 61 which is formula I selected from the group consisting of
- a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or
- b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

## selected from the group consisting of

- a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p toluene sulphonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and
- b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

## 52. (Canceled)

- 53. (Currently Amended) A compound of claim 38 which is a pharmaceutically acceptable salt of a compound of formula I claim 38 which is
- a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or
- b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

## selected from the group consisting of

- a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p toluene sulphonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and
- b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.
- 54. (Currently Amended) A compound of claim 39 which is a pharmaceutically acceptable salt of a compound of formula I of claim 39 which is
- a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid,

trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

## selected from the group consisting of

- a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p toluene sulphonic acid (tosylate salt), 1 napthalene sulfonic acid, 2 napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and
- b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.
- 55. (Original) A pharmaceutical composition for the treatment of a cancerous cell growth mediated by raf kinase comprising a compound of claim 1 or a pharmaceutically acceptable salt of a compound of formula I, and a physiologically acceptable carrier.
  - 56. (Canceled)
  - 57. (Canceled)

- 58. (Original) A pharmaceutical composition of claim 55 wherein the compound of formula I is that defined in claim 38.
- 59. (Original) A pharmaceutical composition of claim 55 wherein the compound of formula I is that defined in claim 39.

## 60. (Canceled)

**61. (Original)** A compound selected from the group consisting of the 3-tert butyl phenyl ureas:

N-(3-tert-butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl urea and N-(3-tert-butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl urea;

the 5-tert-butyl-2-methoxyphenyl ureas:

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(1,3-dioxoisoindolin-5-yloxy)phenyl) urea,

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(1-oxoisoindolin-5-yloxy)phenyl) urea,

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(4-methoxy-3-(N-

methylcarbamoyl)phenoxy)phenyl) urea and

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl) urea;

the 2-methoxy-5-trifluoromethyl)phenyl ureas:

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-

pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-

pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridylthio)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea;

the 4-chloro-3-(trifluoromethyl)phenyl ureas:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea, N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea and N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

the 4-romobromo-3-(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridylthio)phenyl) urea.

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea; and

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

*N*-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N*'-(3-chloro-4-(2-(*N*-methylcarbamoyl)(4-pyridyloxy))phenyl) urea.

62. (Original) A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of Formula I of claim 1.

## 63. (Canceled)

- 64. (Original) A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of Formula I of claim 38.
- 65. (Original) A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of Formula I of claim 39.

## 66. (Canceled)

67. (Original) A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administrating a compound selected from the group consisting of the 3-tert butyl phenyl ureas:

N-(3-tert-butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl urea and N-(3-tert-butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl urea;

the 5-tert-butyl-2-methoxyphenyl ureas:

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(1,3-dioxoisoindolin-5-yloxy)phenyl) urea,

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(1-oxoisoindolin-5-yloxy)phenyl) urea,

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(4-methoxy-3-(N-

methylcarbamoyl)phenoxy)phenyl) urea and

N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl) urea;

```
the 2-methoxy-5-trifluoromethyl)phenyl ureas:
```

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-

pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-

pyridyloxy)phenyl) urea,

urea,

urea:

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridylthio)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(2-methoxy-5-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea;

the 4-chloro-3-(trifluoromethyl)phenyl ureas:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea and N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl)

the 4-romobromo-3-(trifluoromethyl)phenyl ureas:

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-(2-(N-methylcarbamoyl)-4-pyridylthio)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea; and

the 2-methoxy-4-chloro-5-(trifluoromethyl)phenyl ureas:

*N*-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N*'-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(2-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea and

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-N'-(3-chloro-4-(2-(N-methylcarbamoyl)(4-pyridyloxy))phenyl) urea.

- 68. (New) A compound of claim 1 wherein the optional substituents on L<sup>1</sup> are selected from the group consisting of methyl, triflouromethyl, methoxy, Cl and F.
- 69. (New) A compound of claim 1 wherein the optional substituents of B and L are independently selected from the group consisting of methyl, triflouromethyl, ethyl, n-propyl, n-butyl, n-pentyl, tert-butyl, sec-butyl, isobutyl, methoxy, ethoxy, propoxy, Cl, and F.
- 70. (New) A pharmaceutical composition for the treatment of a cancerous cell growth comprising a compound of formula I of claim 1 or a pharmaceutically acceptable salt of a compound of formula I and a physiologically acceptable carrier.

$$A - D - B (I)$$

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of the formula:

-L-M-L<sup>1</sup>,

wherein L is selected from the group consisting of:

(i) phenyl, optionally substituted with substituents independently selected from the group consisting of halogen, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkyl substituted by halogen and C<sub>1</sub>-C<sub>5</sub> alkoxy; or

(ii) pyridinyl optionally substituted with substituents selected from the group consisting of halogen,  $C_1$ - $C_5$  alkyl,  $C_1$ - $C_5$  alkyl substituted by halogen and  $C_1$ - $C_5$  alkoxy;

L<sup>1</sup> comprises a substituted cyclic moiety selected from the group consisting of:

(i) phenyl, substituted with a substituent selected from the group consisting of -C(O)R<sup>c</sup> and -C(O)NR<sup>a</sup>R<sup>b</sup>

and optionally substituted with one or two substituents selected from the group consisting of  $R^7$ ,  $OR^7$  and halogen wherein  $R^7$  is hydrogen,  $C_1$ - $C_5$  alkyl or  $C_1$ - $C_5$  alkyl substituted by halogen, and

(ii) pyridinyl, substituted with a substituent selected from the group consisting of C(O)R<sup>c</sup> and -C(O)NR<sup>a</sup>R<sup>b</sup>

and optionally substituted with one or two substituents selected from the group consisting of  $R^7$ ,  $OR^7$  and halogen, wherein  $R^7$  is hydrogen,  $C_1$ - $C_5$  alkyl or  $C_1$ - $C_5$  alkyl substituted by halogen,

or (iii)

$$NH$$
 or

R<sup>8</sup> is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl,

R<sup>c</sup> is a) hydrogen

- b)  $C_1$ - $C_5$  alkyl, optionally substituted by halogen, hydroxy or  $C_1$ - $C_3$  alkoxy,
- c) phenyl, optionally substituted by halogen, hydroxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>3</sub> alkoxy or CF<sub>3</sub>
- d) pyridinyl, optionally substituted by halogen, hydroxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy or CF<sub>3</sub>;

e) piperiazinyl, optionally substituted by halogen, hydroxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, CF<sub>3</sub> or phenyl, optionally substituted by halogen, -C(O)CH<sub>3</sub>,

wherein R<sup>a</sup> and R<sup>b</sup> independently are

- a) hydrogen,
- b)  $C_1$ - $C_5$  alkyl, optionally substituted by  $CF_3$ , morpholinyl,  $C_1$ - $C_3$  alkoxy, piperidinyl, furyl,  $C_1$ - $C_3$  alkylpyrrolidinyl, -NH-(phenyl), hydroxy, halogen, -OSi( $C_1$ - $C_5$  alkyl) 3 or di ( $C_1$ - $C_4$  alkyl)amino,
- c) phenyl, optionally substituted by halogen,  $di(C_1-C_4 \text{ alkyl})$ amino, morpholinyl, -piperazine(phenyl), optionally substituted by halogen or  $-C(O)CH_3$ ;-piperazine(pyridyl), hydroxy,  $C_1-C_5$  alkyl,  $CF_3$ ,  $C_1-C_3$  alkoxy or -NH-(phenyl),
- d) pyridinyl, optionally substituted by  $-C_1-C_4$  alkoxy, -piperazine(phenyl), optionally substituted by halogen or  $-C(O)CH_3$ , piperazine(pyridyl), hydroxy, halogen,  $C_1-C_5$  alkyl,  $CF_3$ , di $(C_1-C_4$  alkyl)amino, morpholinyl, or -NH-(phenyl),

M is one or two bridging groups selected from the group consisting of -O-, -S-, -C(O)-, -NH-, -CH<sub>2</sub>-, -CH(OH)-, - CHX<sup>a</sup>- and -CX<sup>a</sup><sub>2</sub>-, where X<sup>a</sup> is halogen;

B is selected from the group consisting of:

- (i) phenyl, optionally substituted with substituents independently selected from the group consisting of
  - a) halogen;
- b)  $C_1$ - $C_5$  alkyl, optionally substituted by halogen or -OR<sup>7</sup> wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_5$  alkyl;
  - c) C<sub>1</sub>-C<sub>4</sub> alkoxy, optionally substituted by halogen;
- d) phenyl or -O-phenyl, optionally substituted by -C(O)NHCH<sub>3</sub>,  $C_1$ - $C_5$  alkyl, halogen or -OR<sup>7</sup> wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_5$  alkyl; or
- e) pyrrolyl or pyridinyl, optionally substituted by  $C_1$ - $C_5$  alkyl, halogen or -OR<sup>7</sup> wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_5$  alkyl;

or

(ii) naphthylene optionally substituted with substituents independently selected from the group consisting of

- a) halogen;
- b)  $C_1$ - $C_5$  alkyl, optionally substituted by halogen or -OR<sup>7</sup> wherein R<sup>7</sup> is hydrogen or  $C_1$ - $C_5$  alkyl; or
  - c)  $C_1$ - $C_4$  alkoxy, optionally substituted by halogen.
- 72. (New) A pharmaceutical composition for the treatment of a cancerous cell growth as in claim 70 wherein the pharmaceutically acceptable salt is
- a) a basic salt of an organic acid or an inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or
- b) an acid salt of an organic or inorganic basé containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

## 73. (New) A compound of the formula

A-D-B

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-

B is phenyl substituted by 1-3 substituents,

A is -L-M-L<sup>1</sup>, wherein

L is optionally substituted phenyl,

M is -O- or -S-, and

 $L^1$  pyridinyl substituted by  $C(O)R^aR^b$ , wherein  $R^a$  and  $R^b$  are each independently H,  $C_1$ - $C_{10}$  alkyl or substituted  $C_1$ - $C_{10}$  alkyl.

## 74. (New) A compound as in claim 73 wherein

B is phenyl substituted by 1-3 substituents selected from halogen,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkyl, and  $C_1$ - $C_{10}$  alkyl substituted by halogen up to per-halo, L is unsubstituted phenyl

and  $R^a$  and  $R^b$  are each independently H,  $C_1$ - $C_{10}$  alkyl or substituted  $C_1$ - $C_{10}$  alkyl substituted by OH, -N(CH<sub>3</sub>)<sub>2</sub>, morpholino, -OCH, furan, piperidine, pyridine or -OS<sub>i</sub>(C<sub>3</sub>H<sub>7</sub>)<sub>3</sub>.

75. (New) A compound as in claim 1 wherein B, L and  $L^1$  follow one of the following of combinations:

B= phenyl, L=phenyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B= phenyl, L=pyridinyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B=phenyl, L = naphthyl and  $L^1$  is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B=pyridinyl, L= phenyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B=pyridinyl, L= pyridinyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B =isoquinolinyl, L= phenyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B= isoquinolinyl, L= pyridinyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B= quinolinyl, L= phenyl and  $L^1$  is phenyl, pyridinyl, quinolinyl or isoquinolinyl,

B= quinolinyl, L= pyridinyl and L<sup>1</sup> is phenyl, pyridinyl, quinolinyl or isoquinolinyl.

- 76. (New) A pharmaceutical composition for the treatment of a cancerous cell growth comprising a compound of claim 1 or a pharmaceutically acceptable salt of a compound of formula I and a physiologically acceptable carrier.
- 77. (New) A pharmaceutical composition for the treatment of a cancerous cell growth as in claim 76 wherein the pharmaceutically acceptable salt is
- a) a basic salt of an organic acid or an inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or
- b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

Page 44

78. (New) A compound of Formula I:

**(I)** 

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C (O)-NH-,

A is a substituted moiety of the formula:

 $-L-M-L^1$ ,

wherein

L is selected from the group consisting of phenyl and pyridinyl;

L<sup>1</sup> is selected from the group consisting of phenyl and pyridinyl;

and

M is selected from the group consisting of -O-, -S- and -NHCO-;

wherein L<sup>1</sup> is substituted by -C(O)NR<sub>a</sub>R<sub>b</sub>,

wherein -R<sub>a</sub> and -R<sub>b</sub> are independently:

hydrogen,

 $C_1$ - $C_{10}$  alkyl,

 $C_6$ - $C_{12}$  aryl,

 $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from O, N and S, substituted  $C_{1-10}$  alkyl, substituted  $C_{6-12}$  aryl,

substituted C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, -C<sub>2</sub>H<sub>4</sub>OSi(Pr-i)<sub>3</sub>,

-phenylpiperazine(pyridyl), and

-C<sub>2</sub>H<sub>4</sub>NH(phenyl),

where R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by

- i) halogen up to per halo,
- ii) hydroxy,
- iii)  $C_{1-10}$  alkyl,
- iv)  $C_{1-10}$  alkoxy,
- v)  $-N(CH_3)_2$  and
- vi) C<sub>3-12</sub> cycloalkyl, having 1-3 heteroatoms selected from O, N and S, and

B is selected from the group consisting of:

(i) phenyl and naphthyl, and wherein B is optionally substituted with halogen up to perhalo, and optionally substituted with 1-3 substituents independently selected from the group consisting of

 $OR^7$ ,

 $C_1$ - $C_{10}$  alkyl, up to per-halosubstituted  $C_1$ - $C_{10}$  alkyl,  $C_1$ - $C_{10}$  alkoxy, phenyl.

C<sub>3</sub>-C<sub>12</sub> heteroaryl having 1-3 heteroatoms selected from the group consisting of O, N and S,

-O-phenyl-C(O)NHCH<sub>3</sub>,

and

2,5-dimethyl pyrrolyl

wherein each R<sup>7</sup> is independently

(a)  $C_1$ - $C_{10}$  alkyl,

and

(b) phenyl,

wherein the cyclic structures of B and L bound directly to D are not substituted in the ortho position by -OH.